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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/971,344	11/17/97	GOELET	P

HM31/0414

HOWREY AND SIMON
BOX NO 34
1299 PENNSYLVANIA AVENUE NW
WASHINGTON DC 20004-2402

EXAMINER	
SISSON, B	
ART UNIT	PAPER NUMBER
1641	24

DATE MAILED: 04/14/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/971,344	Philip Goelet et al.
Examiner	**Group Art Unit**
Bradley L. Sisson	1634

☒ Responsive to communication(s) filed on *17 November 1997 and 27 February 1998*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *34-38, 42-44, and 47-50* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *34-38, 42-44, and 47-50* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Location of Application

1. The location of the subject application has changed. The subject application is now located in Technology Center 1600, Group 1630, Art Unit 1634.

Notice of Non-entry of Amendment

2. On 17 November 1997 papers were filed requesting a 37 CFR 1.62 continuation of application 08/216,538 and that the amendment filed on June 17, 1997 under 37 CFR 1.116 be entered. Said Rule 116, which called for (i) the cancellation of "claims 30-32, 40-41, and 45-46" and the addition of new claims 47-49, was entered. On February 27, 1998, a preliminary amendment (Paper No. 23) in the subject application was received. Paper No. 23 calls for (i) the cancellation of "claims 30-33, 40-41, and 45-46;" and (ii) the entry of amendments to claims 34-38, 42, **45**, the entry of "new claims" **47-49**, as well as new claim 50 (emphasis added). No entry of an amended claim 45 has been performed as said claim has been previously canceled. The "new claims" 47-49, as found in the amendment of February 27, 1998 have not been entered as new claims having said numbers were presented, and ultimately entered, in the Rule 116 amendment. Accordingly, those claims which are currently pending in the subject application are 34-38, 42-44, and 47-50.

Attention is also directed to page 1 of the amendment received February 27, 1998 where an amendment to page 33 is requested. Said amendment has NOT been entered as the lines identified

(lines 22-26) do not contain the recited phrase. Upon further inspection of said page 33, it is noted that a similar phrase is found on lines 27 and 28.

Drawings

3. The Figures remain objected to for reasons as stated on the PTO-948 which was attached to Paper No. 14. Applicant is required to submit a proposed drawing correction in response to this Office action. However, correction of the noted defect can be deferred until the application is allowed by the examiner.

Sequence Rule Compliance

4. The subject application has not been found to have been filed with a Sequence Listing and Computer Readable Form (CRF) that lists the sequences disclosed in the subject application AND which appropriately identifies the subject application. See MPEP 2422.05 and the last two sentences of 37 CFR 1.821(e).

Specification

5. The use of the trademark TWEEN 20 has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Acknowledgment is made of applicant's remark at page 7, penultimate paragraph, of the Preliminary Amendment received 27 February 1998 that "applicants have amended the specification to refer to the trademark Tween-20 by its chemical name - polyoxyethylenesorbitan-20-." Upon review of the specification, however, it is noted that not all occurrences of the use of the trademark have been so treated; see page 31, lines 4 and 13. Applicant is urged to carefully review the specification for other occasions where this trademark has been used and to amend the specification accordingly.

Claim Rejections - 35 USC § 112

6. Claims 34-38, 42-44, and 47-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. A review of the originally filed specification fails to provide adequate written support for (i) "selecting said at least two single nucleotide polymorphic sites;"and (ii) "said single nucleotide polymorphic sites is [*sic,* are] within about 150 bases of said genetic trait." A review of claims 30 and 31, as so indicated by applicant as providing support for these limitations, find that one is to select but a single polymorphic site, and then that is one which has to be known

(claim 31), as opposed to starting *de novo*, and sequence fragments of genomic DNA to identify possible useful mutations, determine which correlate with a condition (claim 30). Applicant' reliance upon page 14, lines 13-17 of the specification have not been found to provide adequate support for the concept of single nucleotide polymorphic sites being within about 150 bases of a genetic trait. To facilitate understanding the issue at hand, that portion of the specification identified by applicant as providing support for the now recited claim limitation is reproduced *infra*:

> not be accurate. However, since SNPs [single nucleotide polymorphisms] of the present invention are present in approximately once every 300 bases in the mammalian genome, and exhibit uniformity of distribution, a SNP can, statistically, be found within 150 bases of any particular genetic lesion or mutation. Indeed, the particular mutation may itself be an SNP. (emphasis added)

Upon review of said passage, it is apparent that a given SNP can be statistically predicted to fall within about 150 bases of the next SNP. Given that the distribution of an SNP is "uniform," such SNPs will occur in both coding and non-coding regions. Accordingly, the presence of one mutation falling within 150 bases of another mutaiton does not necessarily speak to, or correlate with a "genetic trait" which is predicated upon the gene of the individual.

Assuming *arguendo*, that the claims were to be amended such that one were to select but an individual SNP, the specification has not been found to provide an adequate written description of those mutations, much less the mutations and their respective flanking sequences, such that the skilled artisan would be able to synthesize primers that would in turn hybridize to regions which flank the SNP(s). It is well settled that "[i]n cases involving unpredictable factors, such as most chemical

reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." See *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970). Here, applicant is seeking protection for a broad method of analyzing DNA of a target human where single nucleotide repeats are compared with a "reference organism" as well as determining whether said target human possesses a genetic trait wherein said determining is predicated upon a correlation between a specific nucleotide mutation and a specific genetic trait. The record admits that such mutations occur with uniform distribution, yet it is anything but certain just which of these mutations could be used to identify whether said target human has any given trait, much less, be capable of correlating with "a reference organism;" the specification teaches analyzing equine genomic sequences for polymorphisms, yet no correlation with mutations in the genomic material of any horse or pony with that of any human has been made.

While the specification presents guidance for the analysis of equine sequences, no such guidance is provided with regard to the testing and evaluation of human sequences. The situation at hand is analogous to that of *Genentech Inc. v. Novo Nordisk A/S* 42 USPQ2d 1001 (CAFC 1997). In *Genentech* the court heard argument that the specification of a patent did not contain sufficient detail concerning the practice of a claimed method (*i.e.*, use cleavable fusion expression to make hGH without undue experimentation); *Ibid*, 1004. As set forth at page 1005:

> Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536. 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out

> the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention....
>
> [2] It is true, as Genentech argues, that a specification need not disclose what is well known in the art. *See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate written description.

Claim 49 and 50 are not adequately supported by the specification for "conditions sufficient to permit a polymerase mediated, template-dependent [primer] extension" and which will permit one to make the requisite comparisons. It is noted with particularity that the claimed method encompasses conditions which allow for virtually any type of amplification product to result. See Sommer and Tautz, *Nucleic Acids Research*. The specification does not set forth a repeatable procedure whereby one of skill in the art would be able to differentiate between the intended and non-intended amplified target nucleic acid sequences. Absence such guidance, the overall operability of the claimed method, especially when non-target sequences are being amplified, could be called into question.

7. Claims 34-38, 42-44, and 47-48 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 47 is indefinite with respect to just what constitutes "a reference organism." Claims 34-38, 42-44, and 48, which depend from claim 47, fail to over come this issue and are similarly indefinite.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978 and whose e-mail address is bradley.sisson@uspto.gov. The examiner can normally be reached on Monday through Thursday from 6:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The fax phone numbers for Group 1630 are (703) 305-3014 and (703) 305-4227.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist for Technology Center 1600 whose telephone number is (703) 308-0196.

B. L. Sisson

BRADLEY L. SISSON
PRIMARY EXAMINER
GROUP ~~1800~~ 1630

4-11-98